```
(FILE 'HOME' ENTERED AT 16:10:09 ON 03 NOV 2005)

     FILE 'MEDLINE, BIOSIS, LIFESCI, EMBASE, SCISEARCH' ENTERED AT 16:13:56 ON
     03 NOV 2005
L1         19553 S MCP-1
L2         16047 S MONOCYTE(A)CHEMOATTRACTANT(A)PROTEIN(A)1
L3          3030 S L1 AND ANTIBOD?
L4          3765 S CCR2
L5           560 S L4 AND ANTIBOD?
L6          5973 S L1 AND RECEPTOR?
L7          1048 S L6 AND ANTIBOD?
L8           166 S L5 AND MONOCLONAL
L9            87 DUP REM L8 (79 DUPLICATES REMOVED)

     FILE 'MEDLINE, BIOSIS, LIFESCI, EMBASE, SCISEARCH' ENTERED AT 16:19:46 ON
     03 NOV 2005
L10           20 S L9 AND PY<=2000

     FILE 'CAPLUS' ENTERED AT 16:25:38 ON 03 NOV 2005
L11           44 S L8
L12           44 DUP REM L11 (0 DUPLICATES REMOVED)
L13           44 S L12
L14           23 S L12 AND PY<=2001
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FILE 'HOME' ENTERED AT 16:10:09 ON 03 NOV 2005

=> file medline biosis lifesci embase scisearch
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                     1.26       1.26
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FILE 'SCISEARCH' ENTERED AT 16:13:56 ON 03 NOV 2005
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=> s mcp-1
L1       19553 MCP-1

=> s monocyte(a)chemoattractant(a)protein(a)1
L2       16047 MONOCYTE(A) CHEMOATTRACTANT(A) PROTEIN(A) 1

=> s L1 and antibod?
L3        3030 L1 AND ANTIBOD?

=> s ccr2
L4        3765 CCR2

=> s L4 and antibod?
L5         560 L4 AND ANTIBOD?

=> s L1 and receptor?
L6        5973 L1 AND RECEPTOR?

=> s L6 and antibod?
L7        1048 L6 AND ANTIBOD?

=> s L5 and monoclonal
L8         166 L5 AND MONOCLONAL

=> dup rem L8
PROCESSING COMPLETED FOR L8
L9           87 DUP REM L8 (79 DUPLICATES REMOVED)

=> d scan L9

L9   87 ANSWERS  BIOSIS  COPYRIGHT (c) 2005 The Thomson Corporation  on STN
TI   Chemoattraction of T cells expressing CCR5, CXCR3 and CX3CR1 by proximal
     tubular epithelial cell chemokines.
IT   Miscellaneous Descriptors
        renal inflammation

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):1

L9   87 ANSWERS  SCISEARCH  COPYRIGHT (c) 2005 The Thomson Corporation  on STN
AN   2004:280474  SCISEARCH
GA   The Genuine Article (R) Number: 803ZO
TI   Experimental arthritis in CC chemokine receptor 2-null mice closely mimics
     severe human rheumatoid arthritis
CC   MEDICINE, RESEARCH & EXPERIMENTAL
STP  KeyWords Plus (R): COLLAGEN-INDUCED ARTHRITIS; II COLLAGEN; T-CELLS; DBA/1
     MICE; INFLAMMATORY ARTHRITIS; MONOCLONAL-ANTIBODIES;
     INFLAMED JOINTS; SYNOVIAL-FLUID; LYMPHOCYTES-T; MOUSE MODEL
     *ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS*
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HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):1

L9    87 ANSWERS  BIOSIS  COPYRIGHT (c) 2005 The Thomson Corporation  on STN
TI    Regulation of basophil chemokine responses by sequential and co-operative
      receptor signalling.
IT    Miscellaneous Descriptors
         basophil chemokine response: regulation; ligand efficacy; receptor
         signalling: co-operative, sequential; receptor usage; Meeting Abstract

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):0

=> d his

     (FILE 'HOME' ENTERED AT 16:10:09 ON 03 NOV 2005)

     FILE 'MEDLINE, BIOSIS, LIFESCI, EMBASE, SCISEARCH' ENTERED AT 16:13:56 ON
     03 NOV 2005
L1         19553 S MCP-1
L2         16047 S MONOCYTE(A)CHEMOATTRACTANT(A)PROTEIN(A)1
L3          3030 S L1 AND ANTIBOD?
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L6          5973 S L1 AND RECEPTOR?
L7          1048 S L6 AND ANTIBOD?
L8           166 S L5 AND MONOCLONAL
L9            87 DUP REM L8 (79 DUPLICATES REMOVED)

=> file medline biosis lifesci embase scisearch
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
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FULL ESTIMATED COST                                     11.54      12.80

FILE 'MEDLINE' ENTERED AT 16:19:46 ON 03 NOV 2005

FILE 'BIOSIS' ENTERED AT 16:19:46 ON 03 NOV 2005
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=> s l9 and py<=2000
L10          20 L9 AND PY<=2000

=> d all L10

L10  ANSWER 1 OF 20     MEDLINE on STN
AN   2000433556     MEDLINE
DN   PubMed ID: 10834607
TI   Chemokine and chemokine receptor expression by liver-derived dendritic
     cells: MIP-1alpha production is induced by bacterial lipopolysaccharide
     and interaction with allogeneic T cells.
AU   Drakes M L; Zahorchak A F; Takayama T; Lu L; Thomson A W
CS   Thomas E. Starzl Transplantation Institute and Department of Surgery,
     University of Pittsburgh Medical Center, PA 15213, USA.
NC   AI41011 (NIAID)
     DK49745 (NIDDK)
SO   Transplant immunology, (2000 Mar) 8 (1) 17-29.
```

Journal code: 9309923. ISSN: 0966-3274.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200009
ED Entered STN: 20000928
Last Updated on STN: 20000928
Entered Medline: 20000921
AB Dendritic cells (DC) are highly-specialized antigen-presenting cells (APC), that initiate and modulate immune responses. Their specialized migratory and tissue-homing properties are regulated by small molecular weight proteins (chemokines) that govern leukocyte migration and activation. Little is known about the capacity of liver DC to produce or respond to chemokines. Here we examined chemokine and chemokine receptor (CR) gene expression in both immature DC progenitors (DCp) and comparatively mature DC generated from mouse liver. Factors affecting production of the chemokine macrophage inflammatory protein (MIP)-1alpha, and the influence of MIP-1alpha on liver DC migration were also investigated. Dendritic cells were propagated in response to granulocyte-macrophage colony stimulating factor (GM-CSF) +/- interleukin (IL)-4 from bone marrow (BM) cells or liver non-parenchymal cells (NPC) isolated from normal mice, or from mice treated with the hematopoietic growth factor Flt3 ligand (FL). Their phenotype and allostimulatory function were assessed by **monoclonal antibody** (mAb) staining and flow cytometry, and by the capacity to induce mixed leukocyte reactions, respectively. Specific chemokine and CR gene expression was studied using the RNase protection assay (RPA). Production of MIP-1alpha was determined by enzyme-linked immunoabsorbent assay (ELISA), and the migratory activity of liver DC induced by MIP-1alpha quantitated using microchemotaxis chambers. Like DC generated simultaneously from BM, liver-derived DC expressed mRNA for a variety of CC and CXC chemokines. RANTES (regulated upon activation, normal T cell expressed and secreted) transcripts were the most strongly expressed. Gene transcripts for the receptor CCR1, that binds RANTES and MIP-1alpha were also readily detected, as was **CCR2**, the receptor for the monocyte chemotactic proteins (MCP)1-4. No major differences in chemokine or CR mRNA expression were detected between immature and more mature liver DC. MIP-1alpha production by liver-derived DC was stimulated by bacterial lipopolysaccharide (LPS), and high levels were also detected in co-cultures of hepatic DC and allogeneic T cells. Chemotactic migration of liver-derived DC was stimulated by MIP-1alpha. Thus, liver-derived DC express mRNA for several CC and CXC chemokines and their receptors that may play key roles in the regulation of hepatic inflammatory responses. Production of MIP-1alpha by liver DC, and their migratory responses to this chemokine, suggest that MIP-1alpha and other chemokines may play significant roles in the regulation of liver DC function and in interactions of liver DC with other leukocytes, under normal and inflammatory conditions.
CT Check Tags: Male
Animals
Bone Marrow Cells: DE, drug effects
Bone Marrow Cells: IM, immunology
Cells, Cultured
Chemotaxis: IM, immunology
Dendritic Cells: DE, drug effects
*Dendritic Cells: IM, immunology
Dendritic Cells: ME, metabolism
Dendritic Cells: SE, secretion
Gene Expression
Humans
Immunophenotyping
Lipopolysaccharides: PD, pharmacology
*Liver: CY, cytology

Liver: IM, immunology
*Macrophage Inflammatory Protein-1: BI, biosynthesis
Macrophage Inflammatory Protein-1: GE, genetics
Macrophage Inflammatory Protein-1: IM, immunology
Macrophage Inflammatory Protein-1: SE, secretion
Mice
Mice, Inbred C3H
Mice, Inbred C57BL
Mitogens: PD, pharmacology
*Receptors, Chemokine: GE, genetics
Research Support, U.S. Gov't, P.H.S.
*T-Lymphocytes: IM, immunology
CN 0 (Lipopolysaccharides); 0 (Macrophage Inflammatory Protein-1); 0 (Mitogens); 0 (Receptors, Chemokine)

=> d L10 bib ab 1-10

L10 ANSWER 1 OF 20 MEDLINE on STN
AN 2000433556 MEDLINE
DN PubMed ID: 10834607
TI Chemokine and chemokine receptor expression by liver-derived dendritic cells: MIP-1alpha production is induced by bacterial lipopolysaccharide and interaction with allogeneic T cells.
AU Drakes M L; Zahorchak A F; Takayama T; Lu L; Thomson A W
CS Thomas E. Starzl Transplantation Institute and Department of Surgery, University of Pittsburgh Medical Center, PA 15213, USA.
NC AI41011 (NIAID)
DK49745 (NIDDK)
SO Transplant immunology, **(2000 Mar)** 8 (1) 17-29.
Journal code: 9309923. ISSN: 0966-3274.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200009
ED Entered STN: 20000928
Last Updated on STN: 20000928
Entered Medline: 20000921
AB Dendritic cells (DC) are highly-specialized antigen-presenting cells (APC), that initiate and modulate immune responses. Their specialized migratory and tissue-homing properties are regulated by small molecular weight proteins (chemokines) that govern leukocyte migration and activation. Little is known about the capacity of liver DC to produce or respond to chemokines. Here we examined chemokine and chemokine receptor (CR) gene expression in both immature DC progenitors (DCp) and comparatively mature DC generated from mouse liver. Factors affecting production of the chemokine macrophage inflammatory protein (MIP)-1alpha, and the influence of MIP-1alpha on liver DC migration were also investigated. Dendritic cells were propagated in response to granulocyte-macrophage colony stimulating factor (GM-CSF) +/- interleukin (IL)-4 from bone marrow (BM) cells or liver non-parenchymal cells (NPC) isolated from normal mice, or from mice treated with the hematopoietic growth factor Flt3 ligand (FL). Their phenotype and allostimulatory function were assessed by **monoclonal antibody** (mAb) staining and flow cytometry, and by the capacity to induce mixed leukocyte reactions, respectively. Specific chemokine and CR gene expression was studied using the RNase protection assay (RPA). Production of MIP-1alpha was determined by enzyme-linked immunoabsorbent assay (ELISA), and the migratory activity of liver DC induced by MIP-1alpha quantitated using microchemotaxis chambers. Like DC generated simultaneously from BM, liver-derived DC expressed mRNA for a variety of CC and CXC chemokines. RANTES (regulated upon activation, normal T cell expressed and secreted) transcripts were the most strongly expressed. Gene transcripts for the

receptor CCR1, that binds RANTES and MIP-1alpha were also readily detected, as was **CCR2**, the receptor for the monocyte chemotactic proteins (MCP)1-4. No major differences in chemokine or CR mRNA expression were detected between immature and more mature liver DC. MIP-1alpha production by liver-derived DC was stimulated by bacterial lipopolysaccharide (LPS), and high levels were also detected in co-cultures of hepatic DC and allogeneic T cells. Chemotactic migration of liver-derived DC was stimulated by MIP-1alpha. Thus, liver-derived DC express mRNA for several CC and CXC chemokines and their receptors that may play key roles in the regulation of hepatic inflammatory responses. Production of MIP-1alpha by liver DC, and their migratory responses to this chemokine, suggest that MIP-1alpha and other chemokines may play significant roles in the regulation of liver DC function and in interactions of liver DC with other leukocytes, under normal and inflammatory conditions.

L10 ANSWER 2 OF 20 MEDLINE on STN
AN 2000430818 MEDLINE
DN PubMed ID: 10828541
TI Expression of multiple functional chemokine receptors and monocyte chemoattractant protein-1 in human neurons.
AU Coughlan C M; McManus C M; Sharron M; Gao Z; Murphy D; Jaffer S; Choe W; Chen W; Hesselgesser J; Gaylord H; Kalyuzhny A; Lee V M; Wolf B; Doms R W; Kolson D L
CS Department of Pathology and Laboratory Medicine University of Pennsylvania Medical Center, Philadelphia, PA 19104, USA.
NC NS0718F (NINDS)
NS35007 (NINDS)
NS37651 (NINDS)
+
SO Neuroscience, **(2000)** 97 (3) 591-600.
Journal code: 7605074. ISSN: 0306-4522.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200009
ED Entered STN: 20000922
Last Updated on STN: 20000922
Entered Medline: 20000914
AB Functional chemokine receptors and chemokines are expressed by glial cells within the CNS, though relatively little is known about the patterns of neuronal chemokine receptor expression and function. We developed **monoclonal antibodies** to the CCR1, **CCR2**, CCR3, CCR6, CXCR2, CXCR3 and CXCR4 chemokine receptors to study their expression in human fetal neurons cultured from brain tissue as well as the clonally derived NT2.N human neuronal cell line (NTera 2/cl.D1). Specific **monoclonal antibody** labeling demonstrated expression of **CCR2**, CXCR2, CXCR3 and CXCR4 on neurons from both sources. Co-labeling studies revealed strong expression of CXCR3 and CXCR4 on both dendritic and axonal processes, with a weaker expression of CXCR2 and **CCR2**. Reverse transcriptase-polymerase chain reaction analysis of pure NT2.N neurons confirmed RNA expression for **CCR2**, CXCR2, CXCR3 and CXCR4. No changes in the neuronal labeling pattern of chemokine receptor expression were noted when NT2.N neurons were grown on a supporting layer of astrocytes, again consistent with similar patterns seen in primary human fetal brain cultures. Analysis of single-cell calcium transients revealed a robust response to stromal derived factor-1alpha (CXCR4) and melanocyte growth-stimulating activity (CXCR2), and variable response to monocyte chemoattractant protein-1 (**CCR2**) or interferon-gamma inducible protein-10 (CXCR3). Finally, we detected the release of monocyte chemoattractant protein-1 from pure cultures of NT2.N neurons, but not undifferentiated NT2 cells.These data indicate that individual neurons may not only co-express multiple functional chemokine

receptors, but also that neurons themselves produce chemokines which may influence cellular function within the central nervous system.

L10 ANSWER 3 OF 20 MEDLINE on STN
AN 2000384102 MEDLINE
DN PubMed ID: 10891427
TI Human endothelial cells express **CCR2** and respond to MCP-1: direct role of MCP-1 in angiogenesis and tumor progression.
AU Salcedo R; Ponce M L; Young H A; Wasserman K; Ward J M; Kleinman H K; Oppenheim J J; Murphy W J
CS Laboratory of Molecular Immunoregulation, Laboratory of Experimental Immunology, Division of Basic Sciences; Intramural Research Support Program, SAIC, Frederick, MD, USA.
SO Blood, **(2000 Jul 1)** 96 (1) 34-40.
Journal code: 7603509. ISSN: 0006-4971.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 200008
ED Entered STN: 20000818
Last Updated on STN: 20020802
Entered Medline: 20000810
AB Although several CXC chemokines have been shown to induce angiogenesis and play roles in tumor growth, to date, no member of the CC chemokine family has been reported to play a direct role in angiogenesis. Here we report that the CC chemokine, monocyte chemotactic protein 1 (MCP-1), induced chemotaxis of human endothelial cells at nanomolar concentrations. This chemotactic response was inhibited by a **monoclonal antibody** to MCP-1. MCP-1 also induced the formation of blood vessels in vivo as assessed by the chick chorioallantoic membrane and the matrigel plug assays. As expected, the angiogenic response induced by MCP-1 was accompanied by an inflammatory response. With the use of a rat aortic sprouting assay in the absence of leukocytic infiltrates, we ruled out the possibility that the angiogenic effect of MCP-1 depended on leukocyte products. Moreover, the direct effect of MCP-1 on angiogenesis was consistent with the expression of **CCR2**, the receptor for MCP-1, on endothelial cells. Assessment of supernatant from a human breast carcinoma cell line demonstrated the production of MCP-1. Treatment of immunodeficient mice bearing human breast carcinoma cells with a neutralizing **antibody** to MCP-1 resulted in significant increases in survival and inhibition of the growth of lung micrometastases. Taken together, our data indicate that MCP-1 can act as a direct mediator of angiogenesis. As a chemokine that is abundantly produced by some tumors, it can also directly contribute to tumor progression. Therefore, therapy employing antagonists of MCP-1 in combination with other inhibitors of angiogenesis may achieve more comprehensive inhibition of tumor growth.

L10 ANSWER 4 OF 20 MEDLINE on STN
AN 2000203438 MEDLINE
DN PubMed ID: 10741397
TI Human intestinal lamina propria and intraepithelial lymphocytes express receptors specific for chemokines induced by inflammation.
AU Agace W W; Roberts A I; Wu L; Greineder C; Ebert E C; Parker C M
CS Division of Rheumatology, Immunology, and Allergy, Brigham and Women's Hospital and Harvard Medical School, Boston, USA..
william.agace@immuno.lu.se
NC DK42166 (NIDDK)
DK52978 (NIDDK)
SO European journal of immunology, **(2000 Mar)** 30 (3) 819-26.
Journal code: 1273201. ISSN: 0014-2980.
CY GERMANY: Germany, Federal Republic of
DT Journal; Article; (JOURNAL ARTICLE)

LA English
FS Priority Journals
EM 200004
ED Entered STN: 20000427
Last Updated on STN: 20020802
Entered Medline: 20000419
AB To determine which chemokine receptors might be involved in T lymphocyte localization to the intestinal mucosa, we examined receptor expression on human intestinal lamina propria lymphocytes (LPL), intraepithelial lymphocytes (IEL) and CD45RO+beta7hi gut homing peripheral blood lymphocytes (PBL). Virtually all LPL and IEL expressed CXCR3 and CCR5, receptors that have been associated with Th1(Tc1)/Th0 lymphocytes, while CCR3 and CCR4, receptors associated with Th2 (Tc2)lymphocytes, CCR7, CXCR1 and CXCR2 were not expressed. CXCR3 and CCR5 receptors were functional, as LPL and IEL migrated to their respective ligands I-TAC and RANTES. In addition, most alphaEbeta7- LPL and IEL expressed high levels of **CCR2**. While the majority of CD45RO(-)beta7hi PBL also expressed CXCR3 and CCR5, a proportion of these cells were CXCR3- and/or CCR5- and some expressed CCR4 and/or CCR7, indicating that lymphocytes recruited to the intestinal mucosa represent a subset of these cells. In summary, our results show that LPL and IEL within the normal intestine express a specific and similar array of chemokine receptors whose ligands are constitutively expressed in the intestinal mucosa and whose expression is up-regulated during intestinal inflammation. These results support the view that CXCR3, CCR5 and **CCR2** may play an important role in lymphocyte localization within the intestinal mucosa.

L10 ANSWER 5 OF 20 MEDLINE on STN
AN 1999410808 MEDLINE
DN PubMed ID: 10479649
TI Expression of **CCR2** by endothelial cells : implications for MCP-1 mediated wound injury repair and In vivo inflammatory activation of endothelium.
AU Weber K S; Nelson P J; Grone H J; Weber C
CS Institut fur Prophylaxe der Kreislaufkrankheiten, Munchen, Germany.. kim.weber@klp.med.uni-muenchen.de
SO Arteriosclerosis, thrombosis, and vascular biology, **(1999 Sep)** 19 (9) 2085-93.
Journal code: 9505803. ISSN: 1079-5642.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199910
ED Entered STN: 19991014
Last Updated on STN: 20020802
Entered Medline: 19991007
AB Endothelial cell proliferation and migration may play a central role in angiogenesis, wound healing, and atherosclerosis. Although CXC chemokines can act on endothelial cells by influencing proliferation, an involvement of CC chemokines and endothelial expression of chemokine receptors remains to be elucidated. Reverse transcription-polymerase chain reaction, RNase protection, Western blot, and flow cytometric analysis showed that human umbilical vein endothelial cells express mRNA and surface protein of the monocyte chemotactic protein-1 (MCP-1) receptor **CCR2**, which was upregulated by inflammatory cytokines. MCP-1 induced migration of endothelial cells in a transwell assay, which was inhibited by the 9-76 MCP-1 receptor antagonist. Increased secretion of MCP-1 or interleukin-8, but not RANTES, on endothelial injury suggested a functional role of **CCR2** in wound repair as measured by ELISA. After mechanical injury to endothelial monolayers, which spontaneously closed within 24 hours, wound repair was delayed by the 9-76 antagonist and by a blocking **monoclonal antibody** to MCP-1, but not to interleukin-8, and was improved by exogenous MCP-1. This was confirmed by quantification

of cell migration into the wound area, whereas proliferation and viability were unaltered by MCP-1 or its analogue. Notably, immunohistochemistry of inflamed tissue revealed **CCR2** staining on arterial, venous, and venular endothelium affected by cellular infiltration. This is the first demonstration of endothelial **CCR2** expression ex vivo, inferring its involvement in inflammatory conditions. Thus endothelial cells express functional **CCR2** that may have important implications for endothelial wound repair and inflammatory reactions.

L10 ANSWER 6 OF 20 MEDLINE on STN
AN 1999199235 MEDLINE
DN PubMed ID: 10097088
TI The chemokine monocyte chemoattractant protein-1 induces functional responses through dimerization of its receptor **CCR2**.
AU Rodriguez-Frade J M; Vila-Coro A J; de Ana A M; Albar J P; Martinez-A C; Mellado M
CS Department of Immunology and Oncology, Centro Nacional de Biotecnologia, Consejo Superior de Investigaciones Cientificas/Universidad Autonoma de Madrid, Campus de Cantoblanco, E-28049 Madrid, Spain.
SO Proceedings of the National Academy of Sciences of the United States of America, **(1999 Mar 30)** 96 (7) 3628-33.
Journal code: 7505876. ISSN: 0027-8424.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199905
ED Entered STN: 19990525
Last Updated on STN: 19990525
Entered Medline: 19990512
AB Cytokines interact with hematopoietin superfamily receptors and stimulate receptor dimerization. We demonstrate that chemoattractant cytokines (chemokines) also trigger biological responses through receptor dimerization. Functional responses are induced after pairwise crosslinking of chemokine receptors by bivalent agonistic antichemokine receptor mAb, but not by their Fab fragments. Monocyte chemoattractant protein (MCP)-1-triggered receptor dimerization was studied in human embryonic kidney (HEK)-293 cells cotransfected with genes coding for the CCR2b receptor tagged with YSK or Myc sequences. After MCP-1 stimulation, immunoprecipitation with Myc-specific **antibodies** revealed YSK-tagged receptors in immunoblotting. Receptor dimerization also was validated by chemical crosslinking in both HEK-293 cells and the human monocytic cell line Mono Mac 1. Finally, we constructed a loss-of-function CCR2bY139F mutant that acted as a dominant negative, blocking signaling through the **CCR2** wild-type receptor. This study provides functional support for a model in which the MCP-1 receptor is activated by ligand-induced homodimerization, allowing discussion of the similarities between bacterial and leukocyte chemotaxis.

L10 ANSWER 7 OF 20 MEDLINE on STN
AN 1999161851 MEDLINE
DN PubMed ID: 10064088
TI Differential immobilization and hierarchical involvement of chemokines in monocyte arrest and transmigration on inflamed endothelium in shear flow.
AU Weber K S; von Hundelshausen P; Clark-Lewis I; Weber P C; Weber C
CS Institut fur Prophylaxe der Kreislaufkrankheiten, Ludwig-Maximilians-Universitat, Munchen, Germany.. kim.weber@klp.med.uni-muenchen.de
SO European journal of immunology, **(1999 Feb)** 29 (2) 700-12.
Journal code: 1273201. ISSN: 0014-2980.
CY GERMANY: Germany, Federal Republic of
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Space Life Sciences
EM 199903

ED Entered STN: 19990326
Last Updated on STN: 20020802
Entered Medline: 19990316

AB Monocyte extravasation into areas of inflammation involves sequential interactions of multiple adhesion molecules. However, differential contribution of chemokines produced by cytokine-stimulated endothelium and their receptors to leukocyte attachment and transmigration under flow conditions remains to be elucidated. The activation of endothelial cells with TNF-alpha up-regulated mRNA and protein expression of the CXC chemokine GRO-alpha and the CC chemokine monocyte chemotactic protein (MCP)-1, which act through the receptors CXCR2 and **CCR2** expressed on monocytes, respectively. Whereas GRO-alpha was immobilized to endothelial cells via heparan sulfate proteoglycans, MCP-1 was secreted in a soluble form. Consequently, inhibition experiments with blocking peptide analogues and **monoclonal antibodies** revealed that GRO-alpha and its receptor CXCR2 but not MCP-1 and its receptors substantially contributed to conversion of rolling into firm, shear-resistant arrest of monocytes to TNF-alpha-stimulated endothelium in physiological flow. In contrast, MCP-1 and **CCR2** but not GRO-alpha and CXCR2 mediated spreading, shape change and subsequent transendothelial migration, which was evident in flow but rarely in stasis and may thus require the establishment of a diffusible MCP-1 gradient. Differential patterns of presentation may determine a functional specialization and hierarchy of chemokines and their receptors in sequential steps of monocyte emigration on inflamed endothelium and shear flow.

L10 ANSWER 8 OF 20 MEDLINE on STN
AN 1998389855 MEDLINE
DN PubMed ID: 9721244
TI The amino terminus of human CCR5 is required for its function as a receptor for diverse human and simian immunodeficiency virus envelope glycoproteins.
AU Hill C M; Kwon D; Jones M; Davis C B; Marmon S; Daugherty B L; DeMartino J A; Springer M S; Unutmaz D; Littman D R
CS Skirball Institute of BioMolecular Medicine, New York University Medical Center, New York, New York, 10016, USA.
NC AI33303 (NIAID)
SO Virology, **(1998 Sep 1)** 248 (2) 357-71.
Journal code: 0110674. ISSN: 0042-6822.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; AIDS
EM 199809
ED Entered STN: 19981006
Last Updated on STN: 19981006
Entered Medline: 19980923

AB The chemokine receptor CCR5 plays a key role in the CD4-dependent entry of human and simian immunodeficiency viruses into target cells. We have mapped the interaction sites on CCR5 for a number of novel anti-CCR5 **monoclonal antibodies** and have used these to study the role of the CCR5 N-terminal ectodomain in viral entry and to demonstrate differential CCR5 epitope expression on different cell types. Deletions of the CCR5 amino terminal domain or substitution with equivalent regions from other chemokine receptors did not affect cell surface expression or reactivity with loop-specific **antibodies**, suggesting that the loop regions remained conformationally intact. Exchanges of the amino terminal segment of CCR5 with the equivalent domains of CCR1, **CCR2**, and CXCR4 did not significantly affect infection with virus pseudotyped with envelope glycoproteins (Envs) from HIV-2 and SIV, but substitution with the CXCR4 sequence abrogated entry mediated by Env from HIV-1. In contrast, deletion of the amino terminus abrogated CCR5 receptor activity for all viral Envs examined. These data indicate that the amino terminus

of CCR5 has an essential role in entry mediated by diverse viral Envs but that the sequence requirements are more relaxed for the HIV-2 and SIV Envs compared to the HIV-1 Env examined. This suggests that different viral Envs make distinct and specific interactions with the amino terminus of CCR5. Viral Env utilization of CCR5 expressed on 293-T cells does not always correlate with the cellular tropism of the virus, and one possible explanation is that Env-accessible interaction sites on CCR5 differ on different cell types. We therefore analyzed binding of several anti-CCR5 **monoclonal antibodies** to cell lines and primary cells that express this chemokine receptor and found that whereas all **antibodies** bound to CCR5-transfected 293T cells, several did not bind to PBMC. The results suggest that CCR5 undergoes cell type specific structural modifications which may affect interaction with different HIV and SIV envelope glycoproteins.

L10 ANSWER 9 OF 20 MEDLINE on STN
AN 1998282207 MEDLINE
DN PubMed ID: 9616160
TI CD43 interacts with moesin and ezrin and regulates its redistribution to the uropods of T lymphocytes at the cell-cell contacts.
CM Comment in: Blood. 1999 Mar 15;93(6):2128-9. PubMed ID: 10189202
AU Serrador J M; Nieto M; Alonso-Lebrero J L; del Pozo M A; Calvo J; Furthmayr H; Schwartz-Albiez R; Lozano F; Gonzalez-Amaro R; Sanchez-Mateos P; Sanchez-Madrid F
CS Servicio de Inmunologia, Hospital de la Princesa, Universidad Autonoma de Madrid, Madrid, Spain.
NC AR41045 (NIAMS)
SO Blood, **(1998 Jun 15)** 91 (12) 4632-44.
Journal code: 7603509. ISSN: 0006-4971.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 199806
ED Entered STN: 19980713
Last Updated on STN: 20000303
Entered Medline: 19980630
AB Chemokines as well as the signaling through the adhesion molecules intercellular adhesion molecule (ICAM)-3 and CD43 are able to induce in T lymphocytes their switching from a spherical to a polarized motile morphology, with the formation of a uropod at the rear of the cell. We investigated here the role of CD43 in the regulation of T-cell polarity, CD43-cytoskeletal interactions, and lymphocyte aggregation. Pro-activatory anti-CD43 **monoclonal antibody** (MoAb) induced polarization of T lymphocytes with redistribution of CD43 to the uropod and the **CCR2** chemokine receptor to the leading edge of the cell. Immunofluorescence analysis showed that all three ezrin-radixin-moesin (ERM) actin-binding proteins localized in the uropod of both human T lymphoblasts stimulated with anti-CD43 MoAb and tumor-infiltrating T lymphocytes. Radixin localized at the uropod neck, whereas ezrin and moesin colocalized with CD43 in the uropod. Biochemical analyses showed that ezrin and moesin coimmunoprecipitated with CD43 in T lymphoblasts. Furthermore, in these cells, the CD43-associated moesin increased after stimulation through CD43. The interaction of moesin and ezrin with CD43 was specifically mediated by the cytoplasmic domain of CD43, as shown by precipitation of both ERM proteins with a GST-fusion protein containing the CD43 cytoplasmic tail. Videomicroscopy analysis of homotypic cell aggregation induced through CD43 showed that cellular uropods mediate cell-cell contacts and lymphocyte recruitment. Immunofluorescence microscopy performed in parallel showed that uropods enriched in CD43 and moesin localized at the cell-cell contact areas of cell aggregates. The polarization and homotypic cell aggregation induced through CD43 was prevented by butanedione monoxime, indicating the

involvement of myosin cytoskeleton in these phenomena. Altogether, these data indicate that CD43 plays an important regulatory role in remodeling T-cell morphology, likely through its interaction with actin-binding proteins ezrin and moesin. In addition, the redistribution of CD43 to the uropod region of migrating lymphocytes and during the formation of cell aggregates together with the enhancing effect of anti-CD43 **antibodies** on lymphocyte cell recruitment suggest that CD43 plays a key role in the regulation of cell-cell interactions during lymphocyte traffic.

L10 ANSWER 10 OF 20 MEDLINE on STN
AN 1998208279 MEDLINE
DN PubMed ID: 9548499
TI Characterization of the **CCR2** chemokine receptor: functional **CCR2** receptor expression in B cells.
AU Frade J M; Mellado M; del Real G; Gutierrez-Ramos J C; Lind P; Martinez-A C
CS Department of Immunology and Oncology, Centro Nacional de Biotecnologia, Consejo Superior de Investigaciones Cientificas, Campus Cantoblanco, Universidad Autonoma, Madrid, Spain.
SO Journal of immunology (Baltimore, Md. : 1950), **(1997 Dec 1)** 159 (11) 5576-84.
Journal code: 2985117R. ISSN: 0022-1767.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 199804
ED Entered STN: 19980430
Last Updated on STN: 20020802
Entered Medline: 19980420
AB We have derived anti-human **CCR2**-specific mAbs by immunization with synthetic peptides corresponding to **CCR2** sequences presumably involved in the interaction with its ligand(s). The characterization of these mAbs includes the ability to recognize the **CCR2** receptor specifically, as well as the function based on their ability to promote Ca2+ influx or to block MCP-1-induced Ca2+ influx and chemotaxis. One mAb (MCP-1 R02) that is directed to the NH2 terminal domain of the **CCR2** receptor has MCP-1 agonist activity, and two that recognize the third extracellular domain (MCP-1R04 and MCP-1 R05) have MCP-1 antagonist activity. We analyzed the presence of **CCR2** in several PBL and tonsil-derived leukocyte populations and found expression of this receptor in monocytes, activated T cells, and, surprisingly, in B cells. **CCR2** receptor expression in B cells was further corroborated in Southern blot using **CCR2**-specific probes. Moreover, both MCP-1 and the agonist mAb trigger specific B cell migration via a PTX-sensitive mechanism, indicating the presence of a functional **CCR2** receptor in these cells.

=> d l10 bib ab 11-20

L10 ANSWER 11 OF 20 MEDLINE on STN
AN 97386611 MEDLINE
DN PubMed ID: 9239395
TI The amino-terminal domain of the **CCR2** chemokine receptor acts as coreceptor for HIV-1 infection.
AU Frade J M; Llorente M; Mellado M; Alcami J; Gutierrez-Ramos J C; Zaballos A; Real G; Martinez-A C
CS Department of Immunology and Oncology, Centro Nacional de Biotecnologia, Consejo Superior de Investigaciones Cientificas, Universidad Autonoma de Madrid, Campus de Cantoblanco, E-28049 Madrid, Spain.
SO Journal of clinical investigation, **(1997 Aug 1)** 100 (3) 497-502.
Journal code: 7802877. ISSN: 0021-9738.

CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals; AIDS
EM 199709
ED Entered STN: 19970916
Last Updated on STN: 20020802
Entered Medline: 19970904
AB The chemokines are a homologous serum protein family characterized by their ability to induce activation of integrin adhesion molecules and leukocyte migration. Chemokines interact with their receptors, which are composed of a single-chain, seven-helix, membrane-spanning protein coupled to G proteins. Two CC chemokine receptors, CCR3 and CCR5, as well as the CXCR4 chemokine receptor, have been shown necessary for infection by several HIV-1 virus isolates. We studied the effect of the chemokine monocyte chemoattractant protein 1 (MCP-1) and of a panel of MCP-1 receptor (**CCR2**)-specific **monoclonal antibodies** (mAb) on the suppression of HIV-1 replication in peripheral blood mononuclear cells. We have compelling evidence that MCP-1 has potent HIV-1 suppressive activity when HIV-1-infected peripheral blood lymphocytes are used as target cells. Furthermore, mAb specific for the MCP-1R **CCR2** which recognize the third extracellular **CCR2** domain inhibit all MCP-1 activity and also block MCP-1 suppressive activity. Finally, a set of mAb specific for the **CCR2** amino-terminal domain, one of which mimics MCP-1 activity, has a potent suppressive effect on HIV-1 replication in M- and T-tropic HIV-1 viral isolates. We conjecture a role for **CCR2** as a coreceptor for HIV-1 infection and map the HIV-1 binding site to the amino-terminal part of this receptor. This concurs with results showing that the CCR5 amino terminus is relevant in HIV-1 infection, although chimeric fusion of various extracellular domains shows that other domains are also implicated. We discuss the importance of **CCR2** structure relative to its coreceptor role and the role of anti-**CCR2** receptor **antibodies** in the prevention of HIV-1 infection.

L10 ANSWER 12 OF 20 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
AN 2001:299495 BIOSIS
DN PREV200100299495
TI Chemokine receptor expression in acute myeloid leukemia cells.
AU Cignetti, Alessandro [Reprint author]; Vallario, Antonella [Reprint author]; Roato, Ilaria [Reprint author]; Allione, Bernardino; Caligaris-Cappio, Federico [Reprint author]; Ghia, Paolo [Reprint author]
CS Laboratory of Tumor Immunology, Institute for Cancer Research and Treatment (IRCC), Candiolo, TO, Italy
SO Blood, (**November 16, 2000**) Vol. 96, No. 11 Part 1, pp. 116a. print.
Meeting Info.: 42nd Annual Meeting of the American Society of Hematology. San Francisco, California, USA. December 01-05, 2000. American Society of Hematology.
CODEN: BLOOAW. ISSN: 0006-4971.
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
Conference; (Meeting Poster)
LA English
ED Entered STN: 20 Jun 2001
Last Updated on STN: 19 Feb 2002
AB The mechanisms regulating the trafficking of leukemic myeloid blasts from the bone marrow microenvironment to the peripheral blood and vice versa are very poorly understood. There is substantial evidence that the migration of normal hematopoietic progenitor and stem cells is a multi-step process that requires the sequential engagement of specific chemokines and their receptors. Therefore, a differential expression of chemokine receptors (CRs) could account for the peculiar pattern of

invasion and diffusion shown by leukemic cells. It has been reported that some acute myeloid leukemia (AML) cells express CXCR4, which appear to mediate the migration across bone marrow endothelium of leukemic blasts in response to SDF-1. Beside this, very little is known about the expression of other CRs by normal hematopoietic precursors and their malignant counterparts. We have analyzed by FACS the CRs expression profile in AML patients at presentation. The CR expression was evaluated by staining leukemic cells with **monoclonal antibodies** specific for CCR1, **CCR2**, CCR5, CCR6, CCR7, CXCR1 and CXCR4. Fourteen AML patients were studied and, according to the FAB classification, there were 7 patients with M4, 3 with M2, 3 with M1 and 1 patient with M0. Leukemic cells were obtained from the peripheral blood of AML patients and they represented 79 +- 19% of the peripheral blood mononuclear cells. CCR1, CCR4, CCR5 and CCR7 were expressed in 0/14, 0/8, 1/14 and 0/11 of cases analyzed, respectively. In five cases of M4, CCR1 and CCR5 were expressed weakly by monocytic blasts. CCR5 was also expressed in one case by the only M0 tested. **CCR2**, CCR6 and CXCR4 were expressed, with levels of mean fluorescence intensity (MFI) varying from patient to patient, in 11/14, 12/14, 13/14 of cases analyzed, respectively. CXCR1 was expressed in 7/14 of cases analyzed and in 7/7 of the M4 studied, respectively. In 2/7 of the M4 that were found positive for CXCR1, only the monocytic blasts contributed to CXCR1 expression. We found that also normal monocytes, as AML-M4 cells, express **CCR2**, CCR6, CXCR1 and CXCR4. To summarize, in the 14 AML patients studied, leukemic cell expressed **CCR2** and CCR6 but not CCR4 and CCR7. CCR1, CCR5 and CXCR1 were positive predominantly in M4, and particularly in monocytic blasts. To better understand the relevance of these data in relation to the migration and homing of AML cells, we are currently investigating the chemokine-R expression by CD34+ cells, the functional activity of chemokine-R expressed by AML cells and the chemokine production of AML cells.

L10 ANSWER 13 OF 20 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
AN 2001:82763 BIOSIS
DN PREV200100082763
TI Regulation of basophil chemokine responses by sequential and co-operative receptor signalling.
AU Sabroe, Ian [Reprint author]; Hartnell, Adele [Reprint author]; Williams, Timothy J. [Reprint author]; Heinemann, Akos [Reprint author]
CS Leukocyte Biology, BMS Division, Imperial College School of Medicine, London, SW7 2AZ, UK
SO Thorax, (**December, 2000**) Vol. 55, No. Supplement 3, pp. A21. print.
Meeting Info.: Winter Meeting of the British Thoracic Society. Westminster, London, UK. December 13-15, 2000. British Thoracic Society.
CODEN: THORA7. ISSN: 0040-6376.
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LA English
ED Entered STN: 14 Feb 2001
Last Updated on STN: 12 Feb 2002

L10 ANSWER 14 OF 20 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
AN 1999:146044 BIOSIS
DN PREV199900146044
TI Novel pathways for negative regulation of inflammatory cytokines.
AU Mantovani, Alberto [Reprint author]
CS Dep. Immunol. Cell Biol., Ist. Richerche Farmacol. "Mario Negri", Via Eritrea 62, 20157 Milan, Italy
SO Biotecnologia Aplicada, (**July-Sept., 1998**) Vol. 15, No. 3, pp. 137-140. print.
ISSN: 0864-4551.

DT Article
General Review; (Literature Review)
LA English
ED Entered STN: 13 Apr 1999
Last Updated on STN: 13 Apr 1999
AB Inflammatory cytokines act in cascades. Pro and anti-inflammatory signals regulate the production of primary and secondary inflammatory cytokines. A number of studies have investigated the actual role played by the two receptors, RI and RII, in interleukin (IL)-1 signaling. All available evidences, including tissue distribution and **monoclonal antibodies** blocking studies, indicate that IL-1-induced activities are mediated exclusively via the IL-1RI, whereas IL-1RII has no signaling activity and inhibits IL-1 effects by acting as a decoy for IL-1, thus sequestering it and preventing the cytokine from binding to the IL-1RI. IL-1RII may represent a physiological pathway of inhibition of IL-1. Induction of expression and release of the IL-1RII may contribute to the antiinflammatory properties of Th2-derived cytokines and glucocorticoids. Other studies on chemokine receptors show that lipopolysaccharides cause a drastic and rapid downregulation of the expression of **CCR2**, a receptor for macrophage chemotactic proteins (MCP)-1 and -3.

L10 ANSWER 15 OF 20 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights reserved on STN
AN 2001000894 EMBASE
TI Basophil responses to chemokines are regulated by both sequential and cooperative receptor signaling.
AU Heinemann A.; Hartnell A.; Stubbs V.E.L.; Murakami K.; Soler D.; LaRosa G.; Askenase P.W.; Williams T.J.; Sabroe I.
CS Dr. I. Sabroe, Leukocyte Biology Section, Biomedical Sciences Division, Imperial College School of Medicine, South Kensington, London SW7 2AZ, United Kingdom. i.sabroe@ic.ac.uk
SO Journal of Immunology, (15 Dec 2000) Vol. 165, No. 12, pp. 7224-7233.
Refs: 61
ISSN: 0022-1767 CODEN: JOIMA3
CY United States
DT Journal; Article
FS 026 Immunology, Serology and Transplantation
029 Clinical Biochemistry
LA English
SL English
ED Entered STN: 20010105
Last Updated on STN: 20010105
AB To investigate human basophil responses to chemokines, we have developed a sensitive assay that uses flow cytometry to measure leukocyte shape change as a marker of cell responsiveness. PBMC were isolated from the blood of volunteers. Basophils were identified as a single population of cells that stained positive for IL-3Rα (CDw123) and negative for HLA-DR, and their increase in forward scatter (as a result of cell shape change) in response to chemokines was measured. Shape change responses of basophils to chemokines were highly reproducible, with a rank order of potency: monocyte chemoattractant protein (MCP) 4 (peak at <1 nM) ≥ eotaxin-2 = eotaxin-3 ≥ eotaxin > MCP-1 = MCP-3 > macrophage-inflammatory protein-1α > RANTES = MCP-2 = IL-8. The CCR4-selective ligand macrophage-derived chemokine did not elicit a response at concentrations up to 10 nM. Blocking mAbs to **CCR2** and CCR3 demonstrated that responses to higher concentrations (> 10 nM) of MCP-1 were mediated by CCR3 rather than **CCR2**, whereas MCP-4 exhibited a biphasic response consistent with sequential activation of CCR3 at lower concentrations and **CCR2** at 10 nM MCP-4 and above. In contrast, responses to MCP-3 were blocked only in the presence of both mAbs, but not after pretreatment with either anti-**CCR2** or anti-CCR3 mAb alone. These patterns of receptor usage were different from those seen for eosinophils and monocytes. We suggest that cooperation between CCRs might be a mechanism for preferential recruitment of

basophils, as occurs in tissue hypersensitivity responses in vivo.

L10 ANSWER 16 OF 20 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights reserved on STN
AN 1999217796 EMBASE
TI Bacterial superantigens induce down-modulation of CC chemokine responsiveness in human monocytes via an alternative chemokine ligand-independent mechanism.
AU Rahimpour R.; Mitchell G.; Khandaker M.H.; Kong C.; Singh B.; Xu L.; Ochi A.; Feldman R.D.; Pickering J.G.; Gill B.M.; Kelvin D.J.
CS Dr. D.J. Kelvin, John P. Robarts Research Institute, University of Western Ontario, London, Ont. N6G 2V4, Canada. kelvin@rri.on.ca
SO Journal of Immunology, (15 Feb 1999) Vol. 162, No. 4, pp. 2299-2307. Refs: 48
ISSN: 0022-1767 CODEN: JOIMA3
CY United States
DT Journal; Article
FS 026 Immunology, Serology and Transplantation
LA English
SL English
ED Entered STN: 19990708
Last Updated on STN: 19990708
AB Staphylococcal superantigens (SAgs) are very potent T cell mitogens, but they can also activate monocytes by binding directly to MHC class II molecules in a manner independent of TCR coengagement. Induction of proinflammatory cytokines and chemokine expression in monocytes by superantigens has recently been reported. Here we report that superantigen stimulation of human peripheral blood monocytes results in a rapid, dose- dependent, and specific down-regulation of chemokine (macrophage inflammatory protein-1α (MIP-1α), monocyte chemotactic protein-1 and MIP-1β) binding sites (e.g., CCR1, **CCR2**, and CCR5), which correlates with a concomitant hyporesponsiveness of human monocytes to these CC chemokine ligands. This down-regulation occurs 15-30 min following superantigen stimulation and is specific to chemokine receptors, in that binding and responsiveness of monocytes to the chemoattractant formyl-tripeptide FMLP are not affected. We further demonstrate that SAg-induced down-modulation of chemokine binding and monocyte hyporesponsiveness to the chemokines MIP-1α, monocyte chemotactic protein-1, and MIP-1β is mediated through cellular protein tyrosine kinases, and the down-modulation can be mimicked by an MHC class II-specific mAb. Additionally, our observations indicate that SAg-induced loss of chemokine binding and monocyte responsiveness is probably mediated by secreted serine proteinases. Bacterial SAg-induced down-modulation of chemokine responsiveness represents a previously unrecognized strategy by some bacteria to subvert immune responses by affecting the intricate balance between chemokine and chemokine receptor expression and function.

L10 ANSWER 17 OF 20 SCISEARCH COPYRIGHT (c) 2005 The Thomson Corporation on STN
AN 2000:719295 SCISEARCH
GA The Genuine Article (R) Number: 356JY
TI Myocardial expression of CC- and CXC-chemokines and their receptors in human end-stage heart failure
AU Damas J K (Reprint); Eiken H G; Oie E; Bjerkeli V; Yndestad A; Ueland T; Tonnessen T; Geiran O R; Aass H; Simonsen S; Christensen G; Froland S S; Attramadal H; Gullestad L; Aukrust P
CS Univ Oslo, Natl Hosp, Dept Cardiol, Div Heart & Lung Dis, Oslo, Norway (Reprint); Univ Oslo, Natl Hosp, Dept Cardiothorac Surg, Div Heart & Lung Dis, Oslo, Norway; Univ Oslo, Natl Hosp, Internal Med Res Inst, Oslo, Norway; Univ Oslo, Natl Hosp, Dept Med, Sect Clin Immunol & Infect Dis, Oslo, Norway; Univ Oslo, Natl Hosp, Dept Med, Endocrinol Sect, Oslo, Norway; Univ Oslo, Natl Hosp, MSD Cardiovasc Res Ctr, Oslo, Norway; Univ Oslo, Ulleval Hosp, Expt Med Res Inst, Oslo, Norway

CYA Norway
SO CARDIOVASCULAR RESEARCH, (**SEP 2000**) Vol. 47, No. 4, pp. 778-787.
ISSN: 0008-6363.
PB ELSEVIER SCIENCE BV, PO BOX 211, 1000 AE AMSTERDAM, NETHERLANDS.
DT Article; Journal
LA English
REC Reference Count: 39
ED Entered STN: 2000
Last Updated on STN: 2000
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB Objectives: Chemokines regulate several biological processes, such as chemotaxis, collagen turnover, angiogenesis and apoptosis. Based on the persistent immune activation with elevated circulating levels of chemokines in patients with congestive heart failure (CHF), we have hypothesised a pathogenic role for chemokines in the development of CHF. The objective of this study was to examine mRNA levels and cellular localisation of chemokines and chemokine receptors in human CHF. Methods: We examined explanted hearts from ten patients with end-stage heart failure (all chambers) and in ten organ donors using an RNase protection assays and immunohistochemical techniques. Results: Our main findings were: (i) expression of eight chemokine and nine chemokine receptor genes in both failing and nonfailing myocardium, (ii) particularly high mRNA levels of monocyte chemoattractant protein (MCP)-1 and CXC-chemokine receptor 4 (CXCR4), in both chronic failing and nonfailing myocardium, (iii) decreased mRNA levels of MCP-I and interleukin (IL)-8 in the failing left ventricles compared to failing left atria, (iv) decreased chemokine (e.g., MCP-1 and IL-8) and increased chemokine receptor (e.g., **CCR2**, CXCR1) mRNA levels in failing left ventricles and failing left atria compared to corresponding chambers in the nonfailing hearts and (v) immunolocalisation of MCP-1, IL-8 and CXCR4 to cardiomyocytes. Conclusion: The present study demonstrates for the first time chemokine and chemokine receptor gene expression and protein localisation in the human myocardium, introducing a new family of mediators with potentially important effects on the myocardium. The observation of chemokine dysregulation in human end-stage heart failure may represent a previously unknown mechanism involved in progression of chronic heart failure.

L10 ANSWER 18 OF 20 SCISEARCH COPYRIGHT (c) 2005 The Thomson Corporation on STN
AN 2000:454344 SCISEARCH
GA The Genuine Article (R) Number: 322KJ
TI Up-regulation of macrophage inflammatory protein-3 alpha/CCL20 and CC chemokine receptor 6 in psoriasis
AU Homey B; Dieu-Nosjean M C; Wiesenborn A; Massacrier C; Pin J J; Oldham E; Catron D; Buchanan M E; Muller A; Malefyt R D; Deng G; Orozco R; Ruzicka T; Lehmann P; Lebecque S; Caux C; Zlotnik A (Reprint)
CS DNAX Res Inst, 901 Calif Ave, Palo Alto, CA 94304 USA (Reprint); DNAX Res Inst, Palo Alto, CA 94304 USA; Schering Plough, Lab Immunol Res, Dardilly, France; Univ Dusseldorf, Dept Dermatol, D-4000 Dusseldorf, Germany; Inst Nacl Nutr Salvador Zubiran, Mexico City 14000, DF, Mexico
CYA USA; France; Germany; Mexico
SO JOURNAL OF IMMUNOLOGY, (**15 JUN 2000**) Vol. 164, No. 12, pp. 6621-6632.
ISSN: 0022-1767.
PB AMER ASSOC IMMUNOLOGISTS, 9650 ROCKVILLE PIKE, BETHESDA, MD 20814 USA.
DT Article; Journal
LA English
REC Reference Count: 61
ED Entered STN: 2000
Last Updated on STN: 2000
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB Autoimmunity plays a key role in the immunopathogenesis of psoriasis; however, little is known about the recruitment of pathogenic cells to skin

lesions. We report here that the CC chemokine, macrophage inflammatory protein-3 alpha, recently renamed CCL20, and its receptor CCR6 are markedly up-regulated in psoriasis, CCL20-expressing keratinocytes colocalize viith skin-infiltrating T cells in lesional psoriatic skin. PBMCs derived from psoriatic patients show significantly increased CCR6 mRNA levels. Moreover, skin-homing CLA(+) memory T cells express high levels of surface CCR6, Furthermore, the expression of CCR6 mRNA is 100- to 1000-fold higher on sorted CLA(+) memory T cells than other chemokine receptors, including CXCR1, CXCR2, CXCR3, **CCR2**, CCR3, and CCR5, In vitro, CCL20 attracted skin-homing CLA(+) T cells of both normal and psoriatic donors; however, psoriatic lymphocytes responded to lower concentrations of chemokine and showed higher chemotactic responses. Using ELISA as well as real-time quantitative PCR, we show that cultured primary keratinocytes, dermal fibroblasts, and dermal microvascular endothelial and dendritic tells are major sources of CCL20, and that the expression of this chemokine can be induced by proinflammatory mediators such as TNF-alpha/IL-1 beta, CD40 ligand, IFN-gamma, or IL-17, Taken together, these findings strongly suggest that CCL20/CCR6 may play a role in the recruitment of T cells to lesional psoriatic skin.

L10 ANSWER 19 OF 20 SCISEARCH COPYRIGHT (c) 2005 The Thomson Corporation on STN
AN 1999:366966 SCISEARCH
GA The Genuine Article (R) Number: 194PT
TI Chronic inflammation upregulates chemokine receptors and induces neutrophil migration to monocyte chemoattractant protein-1
AU Johnston B; Burns A R; Suematsu M; Issekutz T B; Woodman R C; Kubes P (Reprint)
CS Univ Calgary, Fac Med, Dept Physiol & Biophys, Immunol Res Grp, Calgary, AB T2N 4N1, Canada (Reprint); Baylor Coll Med, Cardiovasc Sci Sect, Dept Med, Houston, TX 77030 USA; Keio Univ, Sch Med, Dept Biochem, Tokyo 1608582, Japan; Dalhousie Univ, Dept Pediat, Div Immunol Rheumatol & Infect Dis, Halifax, NS B3J 3G9, Canada
CYA Canada; USA; Japan
SO JOURNAL OF CLINICAL INVESTIGATION, (**MAY 1999**) Vol. 103, No. 9, pp. 1269-1276.
ISSN: 0021-9738.
PB AMER SOC CLINICAL INVESTIGATION INC, 35 RESEARCH DR, STE 300, ANN ARBOR, MI 48103 USA.
DT Article; Journal
LA English
REC Reference Count: 44
ED Entered STN: 1999
Last Updated on STN: 1999
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB Monocye chemoattractant protein-1 (MCP-1) is a CC chemokine that stimulates monocyte recruitment when injected into tissues of healthy animals. However, the function of this chemokine in models with preexisting inflammation is not known. Therefore, MCP-I was superfused over the mesentery of naive rats or rats with chronic adjuvant-induced vasculitis. MCP-I elicited increased leukocyte transendothelial migration in adjuvant-immunized rats compared with naive animals. Surprisingly, histology revealed that neutrophils constituted the majority of leukocytes recruited in adjuvant-immunized animals. In vitro, MCP-1 was also able to induce chemotaxis of neutrophils isolated from adjuvant-immunized rats but not from naive rats. Flow cytometry revealed novel expression of the CC chemokine receptors CCR1 and **CCR2** on neutrophils from adjuvant-immunized animals. In naive animals, an **antibody** against CD18 blocked leukocyte adhesion and emigration in response to MCP-I. In adjuvant-immunized animals, leukocyte adhesion was reduced by **antibodies** against the alpha(4)-integrin but not by **antibodies** against CD18. However, the CD18 **antibody** did block emigration. To our knowledge, this study is the first to show increased sensitivity to a CC chemokine in a model with preexisting

inflammation, and altered leukocyte recruitment profiles in response to MCP-1. It also demonstrates that CD18 is required for chemokine-induced leukocyte transendothelial migration, independent of its known role in mediating firm adhesion.

L10 ANSWER 20 OF 20 SCISEARCH COPYRIGHT (c) 2005 The Thomson Corporation on STN
AN 1998:168540 SCISEARCH
GA The Genuine Article (R) Number: YY558
TI Abnormalities in monocyte recruitment and cytokine expression in monocyte chemoattractant protein 1-deficient mice
AU Lu B; Rutledge B J; Gu L; Fiorillo J; Lukacs N W; Kunkel S L; North R; Gerard C; Rollins B J (Reprint)
CS Dana Farber Canc Inst, Dept Adult Oncol, 44 Binney St, Boston, MA 02115 USA (Reprint); Dana Farber Canc Inst, Dept Adult Oncol, Boston, MA 02115 USA; Harvard Univ, Sch Med, Childrens Hosp, Perlmutter Lab, Boston, MA 02115 USA; Univ Michigan, Sch Med, Dept Pathol, Ann Arbor, MI 48105 USA; Trudeau Inst Inc, Saranac Lake, NY 12983 USA
CYA USA
SO JOURNAL OF EXPERIMENTAL MEDICINE, (**16 FEB 1998**) Vol. 187, No. 4, pp. 601-608.
ISSN: 0022-1007.
PB ROCKEFELLER UNIV PRESS, 1114 FIRST AVE, 4TH FL, NEW YORK, NY 10021 USA.
DT Article; Journal
LA English
REC Reference Count: 50
ED Entered STN: 1998
Last Updated on STN: 1998
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB Monocyte chemoattractant protein 1 (MCP-1) is a CC chemokine that attracts monocytes, memory T lymphocytes, and natural killer cells. Because other chemokines have similar target cell specificities and because **CCR2**, a cloned MCP-1 receptor, binds other ligands, it has been uncertain whether MCP-1 plays a unique role in recruiting mononuclear cells in vivo. To address this question, we disrupted SCYA2 (the gene encoding MCP-1) and tested MCP-1-deficient mice in models of inflammation. Despite normal numbers of circulating leukocytes and resident macrophages, MCP-1(-/-) mice were specifically unable to recruit monocytes 72 h after intraperitoneal thioglycollate administration. Similarly, accumulation of F4/80+ monocytes in delayed-type hypersensitivity lesions was impaired, although the swelling response was normal. Development of secondary pulmonary granulomata in response to Schistosoma mansoni was blunted in MCP-1(-/-) mice, as was expression of IL-4, IL-5, and interferon gamma in splenocytes. In contrast, MCP-1(-/-) mice were indistinguishable from wild-type mice in their ability to clear Mycobacterium tuberculosis. Our data indicate that MCP-1 is uniquely essential for monocyte recruitment in several inflammatory models in vivo and influences expression of cytokines related to T helper responses.

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FILE 'MEDLINE, BIOSIS, LIFESCI, EMBASE, SCISEARCH' ENTERED AT 16:13:56 ON 03 NOV 2005

L1 19553 S MCP-1
L2 16047 S MONOCYTE(A)CHEMOATTRACTANT(A)PROTEIN(A)1
L3 3030 S L1 AND ANTIBOD?
L4 3765 S CCR2
L5 560 S L4 AND ANTIBOD?
L6 5973 S L1 AND RECEPTOR?
L7 1048 S L6 AND ANTIBOD?
L8 166 S L5 AND MONOCLONAL

L9 87 DUP REM L8 (79 DUPLICATES REMOVED)

FILE 'MEDLINE, BIOSIS, LIFESCI, EMBASE, SCISEARCH' ENTERED AT 16:19:46 ON 03 NOV 2005

L10 20 S L9 AND PY<=2000